FIGURE 1

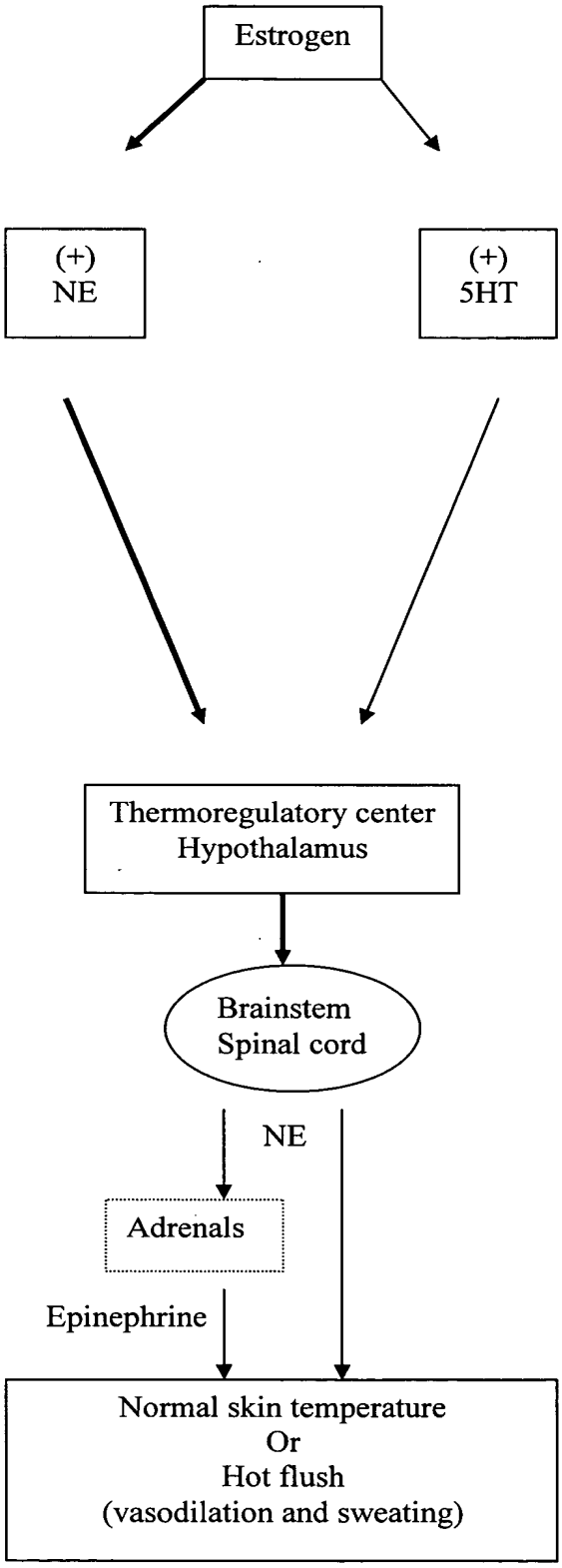

Estrogen
(+)
NE
(+)
5HT
Thermoregulatory center
Hypothalamus
Brainstem
Spinal cord
NE
Adrenals
Epinephrine
Normal skin temperature
Or
Hot flush
(vasodilation and sweating)

FIGURE 2

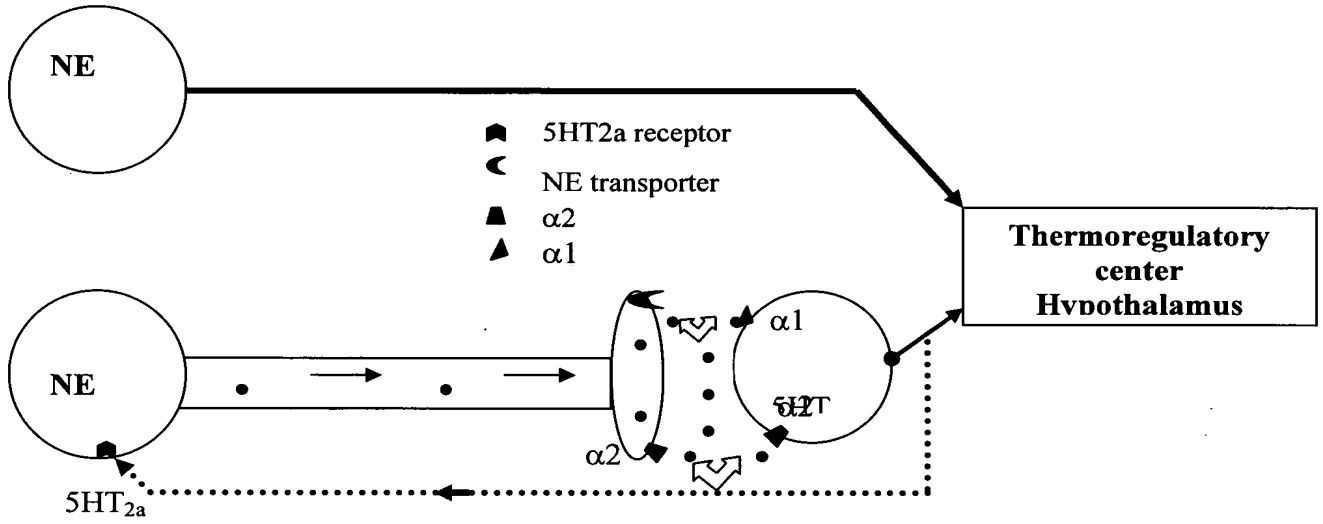
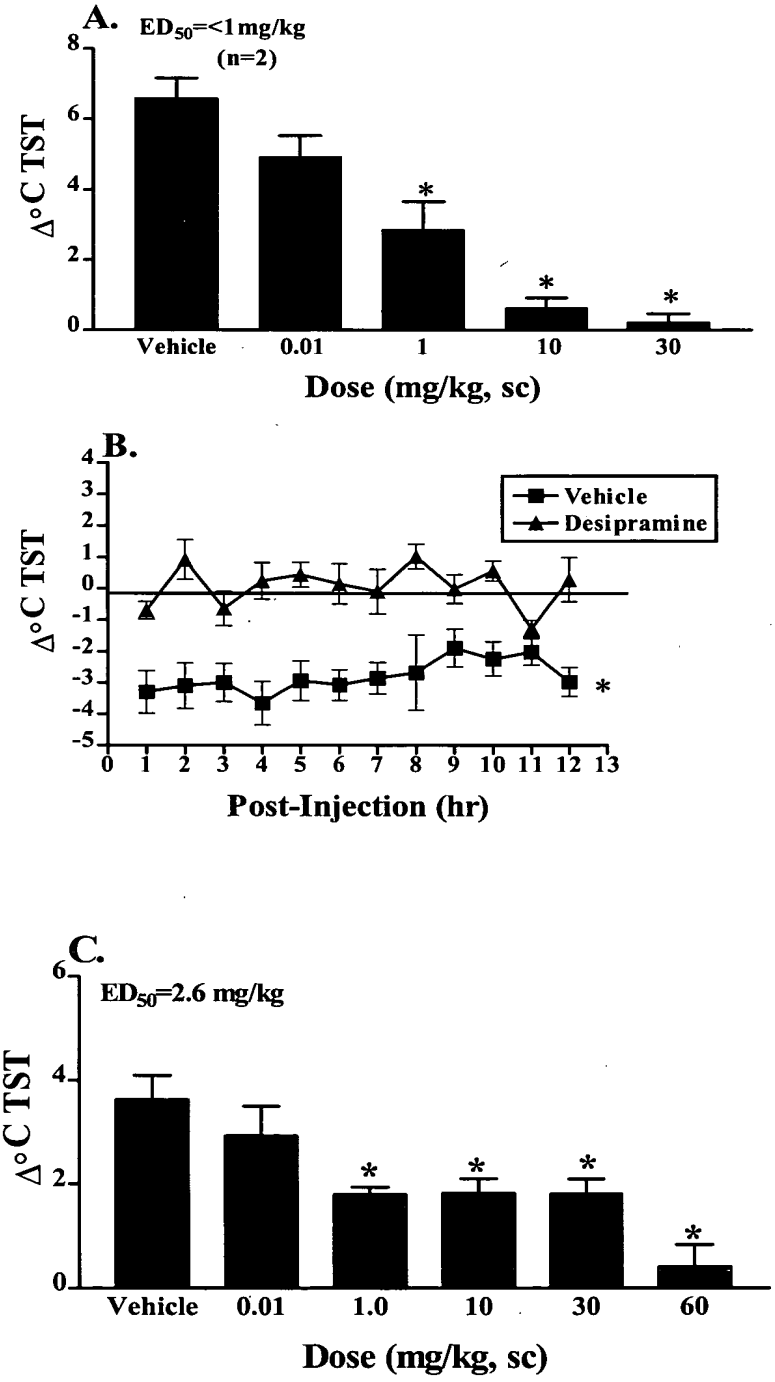
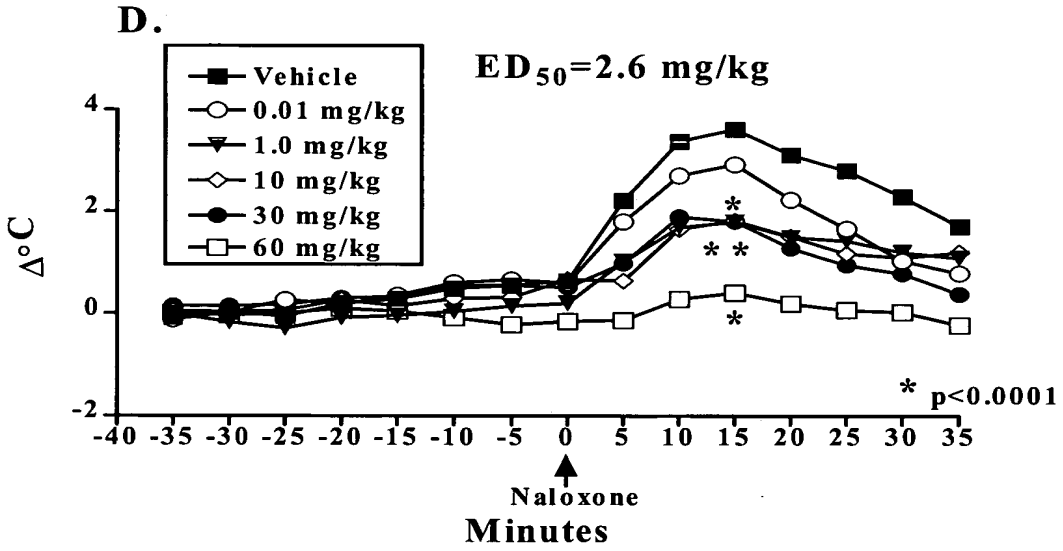
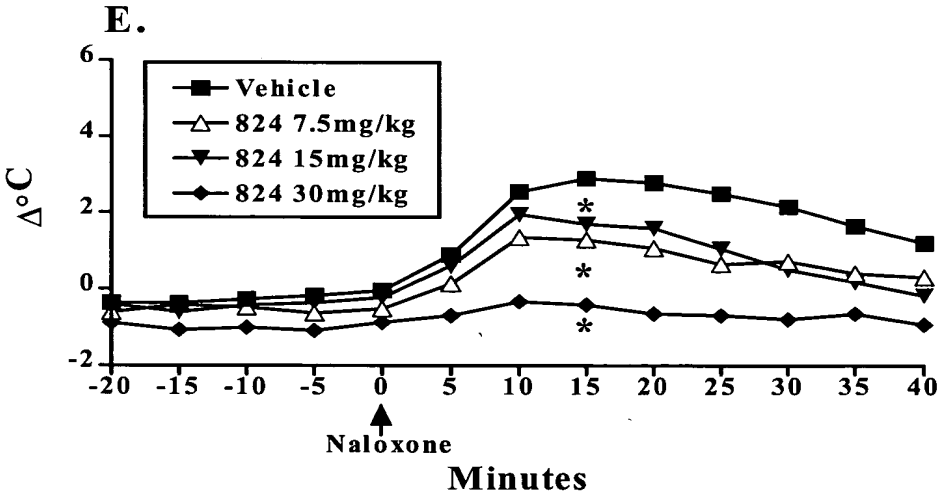

NE
5HT2a receptor
NE transporter
α2
α1
Thermoregulatory center Hypothalamus
NE
α1
α2
5HT2a

FIGURE 3


A.
ED50=<1 mg/kg
(n=2)
Δ°C TST
Vehicle
0.01
1
10
30
Dose (mg/kg, sc)
B.
Vehicle
Desipramine
Δ°C TST
Post-Injection (hr)
C.
ED50=2.6 mg/kg
Δ°C TST
Vehicle
0.01
1.0
10
30
60
Dose (mg/kg, sc)


D.
Vehicle
0.01 mg/kg
1.0 mg/kg
10 mg/kg
30 mg/kg
60 mg/kg
ED50=2.6 mg/kg
Δ°C
4
2
0
-2
* p<0.0001
-40 -35 -30 -25 -20 -15 -10 -5 0 5 10 15 20 25 30 35
Naloxone
Minutes


E.
Vehicle
824 7.5mg/kg
824 15mg/kg
824 30mg/kg
Δ°C
6
4
2
0
-2
-20 -15 -10 -5 0 5 10 15 20 25 30 35 40
Naloxone
Minutes

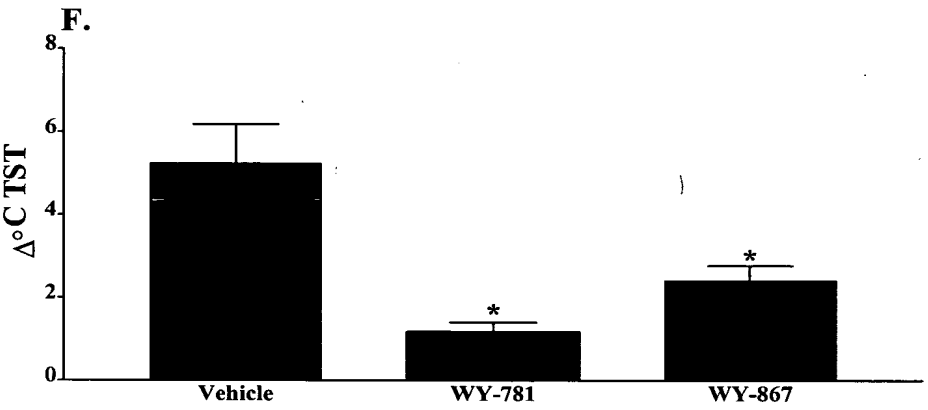

F.
8
6
4
2
0
Δ°C TST
*
*
Vehicle
WY-781
WY-867
(30 mg/kg, sc)

FIGURE 4

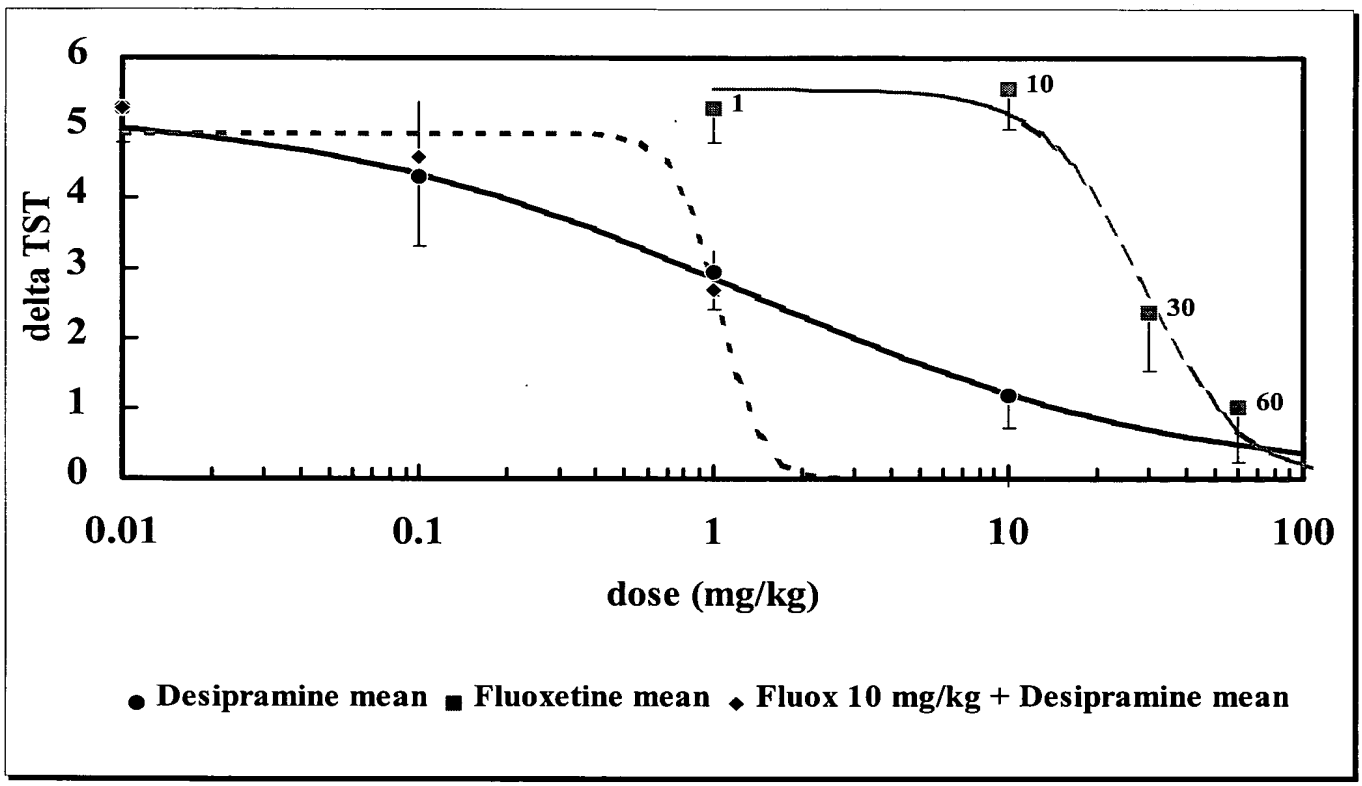
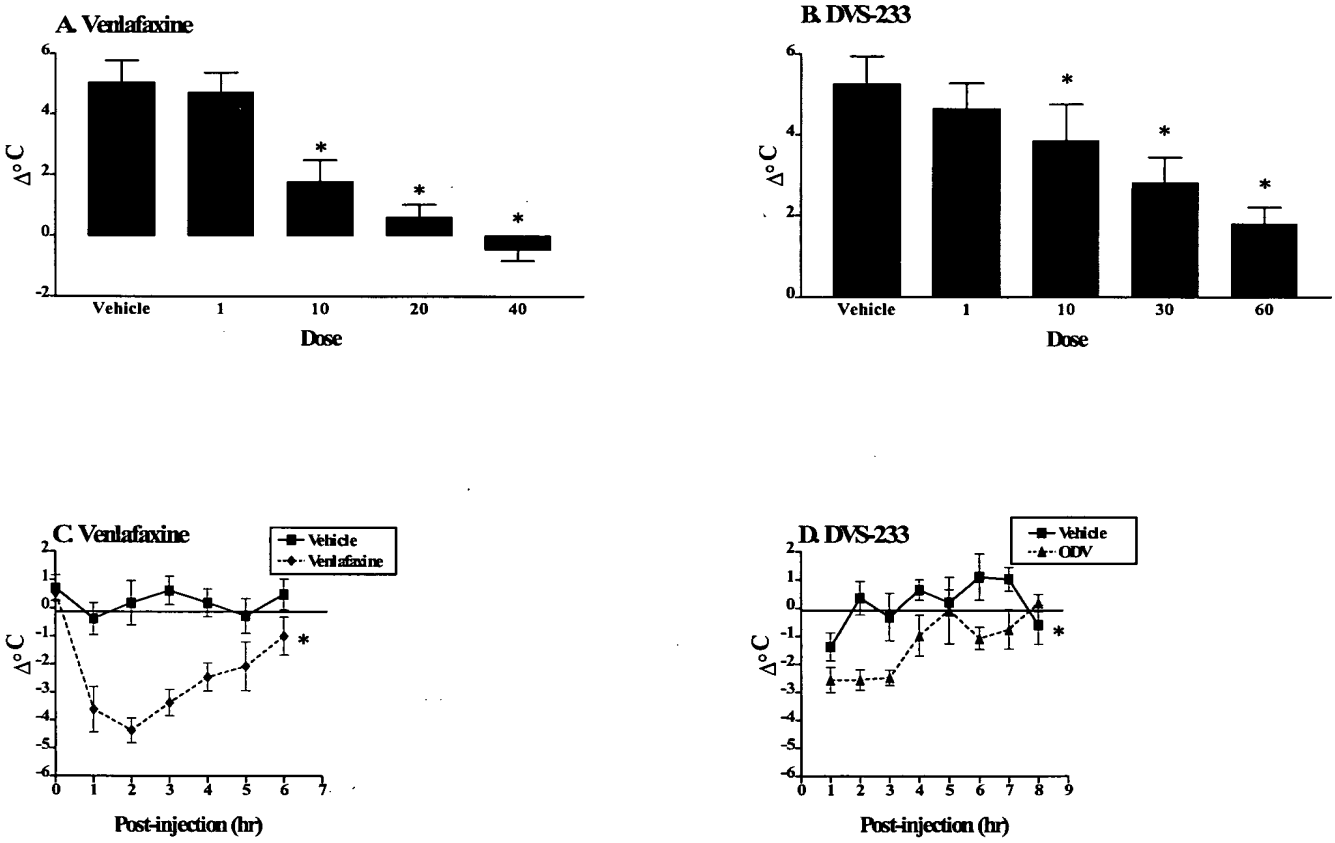
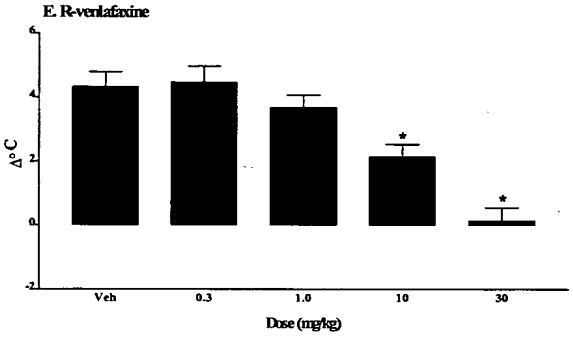
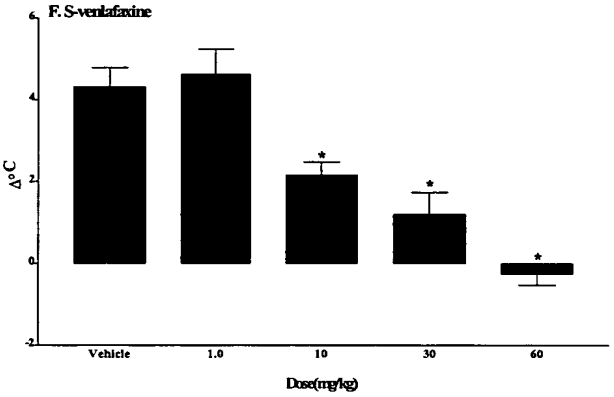
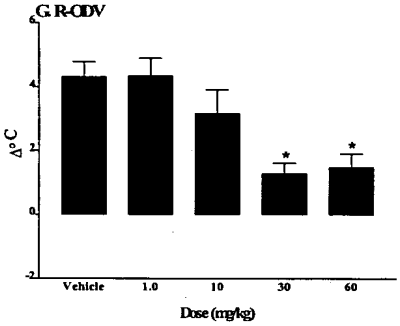

6
5
4
3
2
1
0
delta TST
1
10
30
60
0.01
0.1
1
10
100
dose (mg/kg)
● Desipramine mean ■ Fluoxetine mean ◆ Fluox 10 mg/kg + Desipramine mean

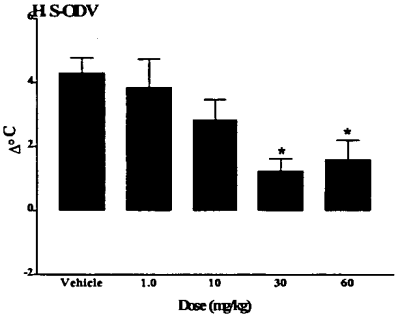
FIGURE 5


A. Venlafaxine
Δ°C
Vehicle
1
10
20
40
Dose
B. DVS-233
Δ°C
Vehicle
1
10
30
60
Dose
C. Venlafaxine
Vehicle
Venlafaxine
Δ°C
Post-injection (hr)
D. DVS-233
Vehicle
ODV
Δ°C
Post-injection (hr)


E. R-venlafaxine
Δ°C
Veh
0.3
1.0
10
30
Dose (mg/kg)


F. S-venlafaxine
Δ°C
Vehicle
1.0
10
30
60
Dose(mg/kg)


G. R-ODV
Δ°C
Vehicle
1.0
10
30
60
Dose (mg/kg)


H. S-ODV
Δ°C
Vehicle
1.0
10
30
60
Dose (mg/kg)

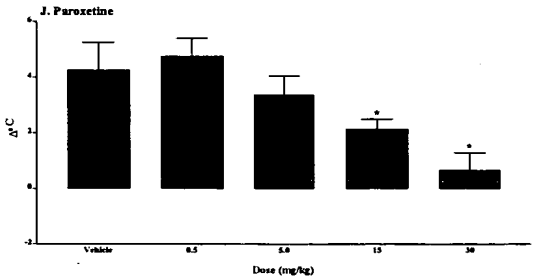
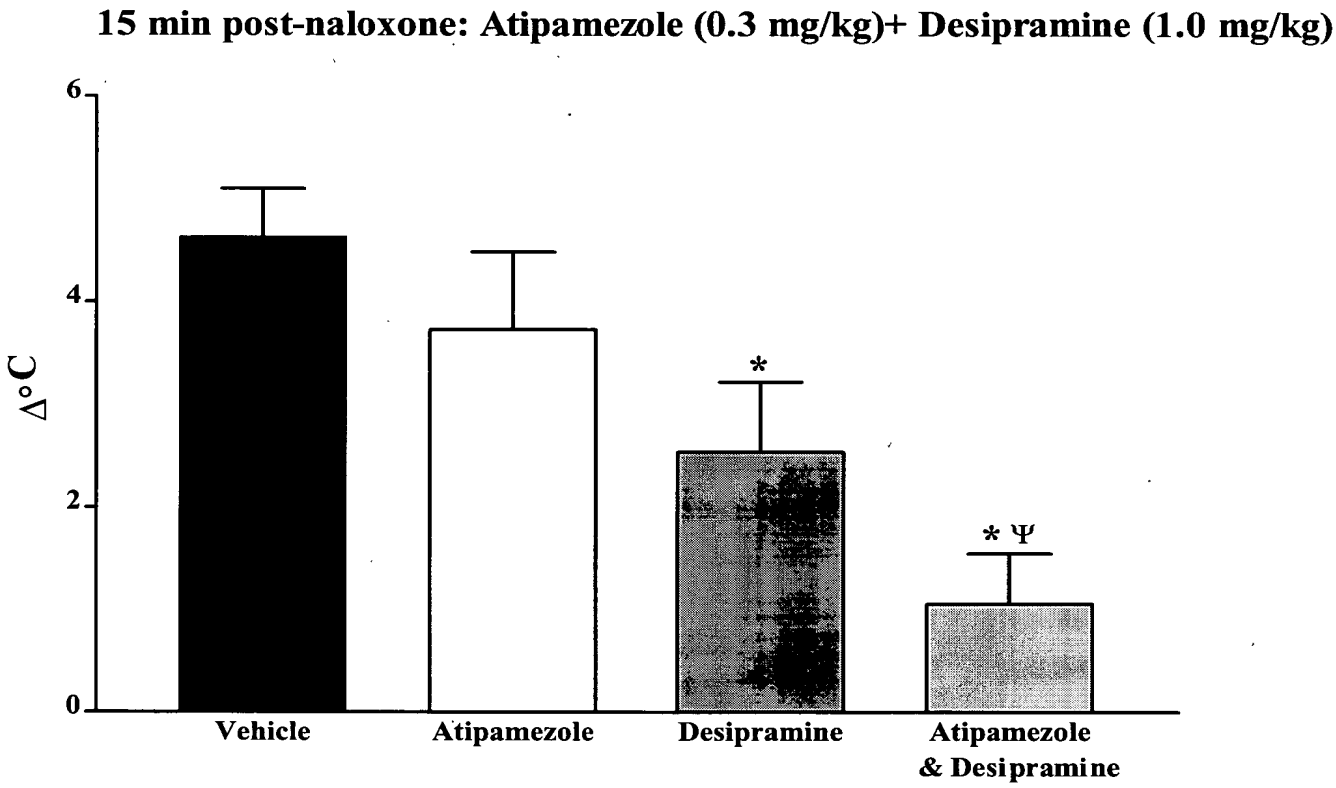

J. Paroxetine
Δ°C
Vehicle
Dose (mg/kg)

FIGURE 6


15 min post-naloxone: Atipamezole (0.3 mg/kg)+ Desipramine (1.0 mg/kg)
Δ°C
6
4
2
0
*
* Ψ
Vehicle
Atipamezole
Desipramine
Atipamezole & Desipramine